

Nucleophilic Aromatic Substitution Reactions of Chloroazines with Bisulfide (HS^-) and Polysulfides (S_n^{2-})

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Reactions of bisulfide and polysulfides with chloroazines (important constituents of agrochemicals and textile dyes) were examined in aqueous solution at 25 °C. For atrazine, rates are first-order in polysulfide concentration, and polysulfide dianions are the principal reactive nucleophiles; no measurable reaction occurs with HS^- . Second-order rate constants for reactions of an array of chloroazines with polysulfides are several orders of magnitude greater than for reactions with HS^- . Transformation products indicate the substitution of halogen(s) by sulfur. Ring aza nitrogens substantially enhance reactivity through a combination of inductive and mesomeric effects, and electron-withdrawing or electron-donating substituents markedly enhance or diminish reactivity, respectively. The overall second-order nature of the reaction, the products observed, and reactivity trends are all consistent with a nucleophilic aromatic substitution ($\text{S}_\text{N}\text{Ar}$) mechanism. Rate constants for reactions with HS^- and S_n^{2-} ($n = 2-5$) correlate only weakly with lowest unoccupied molecular orbital energies, suggesting that the electrophilicity of a chloroazine is not the sole determinant of its reactivity. When second-order rate constants are extrapolated to HS^- and S_n^{2-} concentrations reported in salt marsh porewaters, half-lives of minutes to years are obtained. Polysulfides in particular could play an important role in effecting abiotic transformations of chloroazines in hypoxic marine waters.

Introduction

The monochloro-*s*-triazine agrochemicals are extensively used in the United States as pre-emergence herbicides to control broadleaf weeds and some annual grasses, primarily in corn and soybean crops. Atrazine, simazine, and cyanazine together represent 18% (by weight of active ingredient) of pesticide use in U.S. agriculture (1). These herbicides undergo discharge to the surface waters of sensitive coastal marine environments (such as the Chesapeake Bay and surrounding salt marshes) via nonpoint atmospheric (2), fluvial (3, 4), and groundwater (5) routes and are potentially of (eco)-toxicological concern (6) in such regions.

Chloroazines are not only used as herbicides; the dichloro-*s*-triazine agrochemical anilazine was, until recently, used as a fungicide. Haloazines are also important constituents of fiber-reactive textile dyes. Approximately 19% of total dye production in 1991 consisted of fiber-reactive dyes (7), a sector

of the market that is rapidly growing. It has been estimated that 10–50% of industrial production of fiber-reactive dyes is released to receiving surface waters (8).

Chloroazines are, hence, frequently emitted to coastal marine environments, which may also contain high concentrations of hydrogen sulfide species (H_2S and HS^-) and polysulfides (S_n^{2-} , where $n = 2-5$). These reduced sulfur species are produced via dissimilatory microbial sulfate reduction under hypoxic conditions. Concentrations of hydrogen sulfide and polysulfides in coastal marine sediment porewaters have been reported as high as 5.6 and 0.33 mM, respectively (9, 10). The potential therefore exists for such highly reactive reduced sulfur nucleophiles to serve as environmental “reagents” effecting the abiotic degradation of chloroazines.

A wealth of data exists in the literature pertaining to bimolecular substitution ($\text{S}_\text{N}2$) reactions of environmental nucleophiles (including reduced sulfur species) with halogenated aliphatic substrates (11–15). Some studies (13, 14) have shown polysulfides to be considerably more reactive nucleophiles than HS^- , to the point that although polysulfides are typically less abundant than HS^- , their contribution to overall rates of $\text{S}_\text{N}2$ reactions can nonetheless exceed that of HS^- at $\text{pH} > 7$. Chloroazines, which contain $\text{sp}^2\text{-Cl}$ carbon–halogen bonds, are however subject to reactions via a very different pathway, namely, nucleophilic aromatic substitution ($\text{S}_\text{N}\text{Ar}$). Atrazine may, for example, react with a sulfur nucleophile via $\text{S}_\text{N}\text{Ar}$ through a negatively charged addition intermediate (Meisenheimer or σ complex) to form a sulfur-substituted azine product (Scheme 1). The formation of the σ complex is a highly unfavorable process, as disruption of the aromatic π system is required; the first step is therefore typically rate-determining (16). The ring aza nitrogens, in addition to electron-donating or electron-withdrawing substituents that may be present, can affect the stability of the σ complex through mesomeric and inductive effects (17). The number, type, and position of substituents, hence, greatly influence the reactivity of haloazines toward nucleophilic displacement.

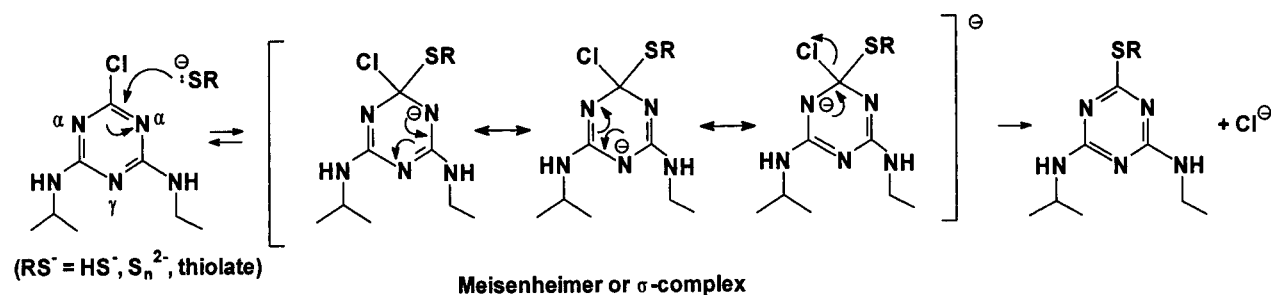
Studies of $\text{S}_\text{N}\text{Ar}$ reactions of haloazines in aqueous solution have received minimal attention and have focused primarily on alkaline hydrolysis, relevant to the application of reactive dyeing processes (18, 19). With only few exceptions (e.g., hydrolysis of atrazine, trinitrotoluene (TNT), and related species; see refs 20 and 21), $\text{S}_\text{N}\text{Ar}$ reactions have been largely overlooked by environmental scientists. In fact, two environmental organic chemistry texts (22, 23) fail altogether to mention this reaction, an indication of the paucity of past studies on this topic in the environmental literature.

Only limited research has been reported for nucleophilic displacement reactions of activated aromatic substrates with reduced sulfur species in aqueous solution. Previous researchers noted that polysulfide salts converted ^{14}C -labeled simazine [2-chloro-4,6-bis(ethylamino)-*s*-triazine-2,4,6- ^{14}C] residues in soil to a chloroform-insoluble charcoal-adsorbable degradate (24). The rates, products, and mechanisms involved were not investigated. The absence of data pertaining to $\text{S}_\text{N}\text{Ar}$ reactions of sulfur nucleophiles with heteroaromatic contaminants in water at ambient temperatures prompted the present investigation.

The primary purpose of this research was to explore the potential impact of reduced sulfur nucleophiles (HS^- and polysulfides) on the abiotic transformation of chloroazine agrochemicals, especially atrazine. The effects of nucleophile concentration, identity, and acid/base speciation on rates of atrazine reaction were systematically investigated in relatively

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SCHEME 1



well-defined solutions at 25 °C so as to determine the relevant second-order rate constant(s). Products were characterized by gas chromatography/mass spectrometry (GC/MS) following methylation or pentafluorobenzoylation. The influence of chloroazine structure on reactivity was explored by measuring the rates and products of reactions of HS⁻ and S_n²⁻ with a series of 10 additional structurally related haloazines. This information provides a consistent database of rate constants that was used to test structure–activity relationships (SARs). The results can be incorporated in fate and exposure assessment models in order to predict environmental risk associated with discharge of chloroazines to coastal marine environments.

Experimental Section

Reagents. All triazine agrochemicals were obtained from Chem Service. All chloropyridines, chloropyrimidines, chloroquinoxalines, and chlorobenzenes were obtained from Aldrich. All chemicals were used as received. Fluorotriazine [2-fluoro-4-(isopropylamino)-6-(ethylamino)-s-triazine] was synthesized specifically for this study (25). Standard solutions of haloazines were prepared either in toluene, in *n*-hexane, or in chloroform (ultraresianalyzed grade; J.T. Baker) for gas chromatographic (GC) or combined gas chromatographic/mass spectrometric (GC/MS) analysis. Stock solutions for spiking aqueous samples were prepared in argon-sparged methanol (ultraresianalyzed grade; J.T. Baker) or tetrahydrofuran (THF; ultraresianalyzed grade; Fluka).

Na₂S stock solutions were prepared with Na₂S·9H₂O (98–103%; J.T. Baker), HCl (J.T. Baker), and deoxygenated high-purity (> 15 MΩ·cm) deionized distilled water obtained from a Milli-Q Plus UV water system (Millipore Corp.). Details pertaining to preparation of these solutions are provided by Lippa (25). Solutions were analyzed for trace polysulfide contamination using the triphenylphosphine method described below.

Polysulfide solutions were prepared in two ways: (1) via equilibration of HS⁻ solution with excess cyclooctasulfur (S₈, >99.9%; Fluka) and (2) via dissolution of purified sodium tetrasulfide crystals (Na₂S₄, 90+% technical grade; Alfa). Na₂S₄ crystals were purified by rinsing with deoxygenated toluene to remove excess elemental sulfur contamination and were then dried under nitrogen. The solutions were equilibrated under an N₂/H₂ atmosphere at room temperature while undergoing constant stirring for 6 months.

Analysis of Reduced Sulfur Species. The total hydrogen sulfide content [H₂S]_T of bisulfide solutions, representing the sum of all hydrogen sulfide species ([H₂S] + [HS⁻] + [S²⁻]), was measured by iodometric titration. Bisulfide ion concentrations were computed from [H₂S]_T and pH values measured with a Fisher AP63 Accumet pH/mV/ion meter and an Orion Ross combination pH electrode, using ionization constants (26) that were corrected for ionic strength through activity coefficients determined from the Davies approximation.

The total reduced sulfur content [S(–II)]_T of polysulfide solutions represents the sum of [H₂S]_T and [H₂S_n]_T, where the latter represents the total concentration of polysulfides, hydropolysulfides, and sulfanes numerically equal to Σ([S_n²⁻] + [HS_n⁻] + [H₂S_n]) for *n* = 2–5. For these solutions, [S(–II)]_T was measured by iodometric titration.

Methods appropriate for determining concentrations of individual polysulfide species in complex matrixes have not, to the best of our knowledge, been developed. In this and related research (25), polysulfide concentrations were determined by a modification of the triphenylphosphine method previously developed by Borchardt and Easty (27). The results yield [S(0)]_{poly}, the dissolved S(0) concentration contributed by polysulfides (equivalent to (n – 1)·[H₂S_n]_T). Knowledge of the average chain length as a function of pH from published equilibrium constants (28–30) then enables the computation of the total concentration of polysulfide dianions Σ[S_n²⁻] and hydropolysulfides Σ[HS_n⁻].

Experimental Systems. Reaction kinetics were measured under pseudo-first-order conditions whenever possible, with initial haloazine concentrations typically only 1% of that of the reduced sulfur nucleophile. Exceptions occurred for reactions of polysulfides with anilazine, tetrachloroquinoxaline (TCQ), and tetrachloropyrimidine (TCPm), for which reactions were too rapid to be experimentally accessible at such high ratios of polysulfide to haloazine. Solutions were prepared in an anaerobic glovebox and were spiked with aliquots (50–500 μL) of MeOH or THF containing the appropriate azine, yielding initial haloazine concentrations ranging from 10 to 35 μM. Reactors were vigorously mixed for 30 s in the glovebox and were incubated in a water bath at 25.0 ± 0.1 °C. Aliquots were periodically extracted into *n*-hexane (or chloroform in the case of cyanazine), followed by analysis via GC or GC/MS.

Pseudo-first-order rate constants were obtained by performing a linear regression of the natural logarithm of haloazine concentration versus time. Except for experiments involving anilazine, TCQ, and TCPm, reactions were monitored over sufficient time (2–3 half-lives) to verify pseudo-first-order kinetics. Reactions of polysulfides with anilazine and TCPm proceeded too rapidly to enable collection of sufficient data to confirm pseudo-first-order behavior (in fact, TCPm had reacted to below detection limit by the time the first sample was extracted 10 s after initiating the experiment), and reaction of TCQ with polysulfides evinced a marked slowing over time that was attributed to the depletion of polysulfides at the low ratios of polysulfides/haloazine employed. For anilazine and TCQ, pseudo-first-order rate constants were estimated from initial rate data. For selected atrazine experiments, second-order rate constants in the presence of multiple reactive nucleophiles (e.g., S_n²⁻, HS_n⁻, and OH⁻) were concurrently determined for several experiments with varying nucleophile concentrations. These data were analyzed via nonlinear regression techniques using Scientist for Windows, version 2.01 (MicroMath Scientific Software, Salt Lake City, UT).

Derivatization Methods. All azine transformation products were methylated using CH_3I (Aldrich, 99%). A 1-mL aliquot of spent reaction mixture (containing up to 35 μM azine product and up to 34 mM $[\text{S}(-\text{II})]_{\text{T}}$) was added to approximately 2 mL of deoxygenated solution containing excess CH_3I ($>0.1\text{ M}$) in $\text{Na}_2\text{B}_4\text{O}_7$ buffer (20 mM; pH 9.0). This mixture was heated at 60 $^\circ\text{C}$ in a water bath for 1 h and, after cooling to room temperature, was extracted with *n*-hexane. Aliquots (1 mL) of selected polysulfide solutions were methylated with 200 μL of neat CH_3I , followed by heating, cooling to room temperature, and extraction into pentane.

Atrazine and cyanazine transformation products were also pentafluorobenzylated using pentafluorobenzyl bromide (PFBBBr; Aldrich, 99+%). Approximately 10 mg of phase transfer catalyst, benzyltrimethyltetradecylammonium chloride ($>99.0\%$; Fluka), was added to a 1-mL aliquot of exhausted reaction mixture, to which 1 mL of 5% PFBBBr (v/v) in toluene was added. The mixture was heated to 60 $^\circ\text{C}$ in a water bath for 1 h with 1 min of vigorous mixing every 10 min. The solution was centrifuged for 10 min at 3500 rpm, and the resulting toluene phase (containing derivatized product) was dried with anhydrous sodium sulfate.

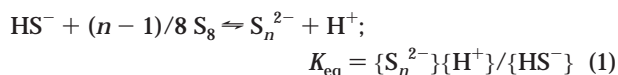
Gas Chromatographic Analysis. *n*-Hexane extracts containing haloazines were analyzed using a Carlo-Erba Mega 2 series GC equipped with a flameless nitrogen–phosphorus detector (NPD), a cold on-column injector and a DB-5 column (30 m \times 0.25 mm \times 0.25 μm film thickness; J&W Scientific). Toluene extracts for $[\text{S}(0)]_{\text{poly}}$ analysis were analyzed with the same column and injector and a flame-ionization detector (FID). Chloroform extracts and selected *n*-hexane extracts were analyzed via GC/MS (ThermoQuest Trace 2000 gas chromatograph coupled to a Finnigan quadrupole mass spectrometer) using on-column injection and a DB-200 column (trifluoropropyl polysiloxane bonded phase; 30 m \times 0.25 mm \times 0.25 μm film thickness; J&W Scientific). Electron impact (EI) mass spectra were obtained in both full-scan and selected ion monitoring (SIM) modes.

Derivatized transformation products were analyzed via GC/MS. Modes for MS analyses of products included electron impact (EI), positive chemical (PCI), and negative chemical (NCI) ionization techniques using methane (CH_4 , 99.995%) as a reagent gas for CI. PCI spectra were generated using an electron energy of 70 eV and an emission current of 350 μA . The CH_4 flow during PCI was set to produce an initial reagent ion ratio for the ions m/z 17 $^+$, 29 $^+$, and 41 $^+$ of 1/1/0.25, respectively, although this ratio does drift somewhat during analysis. NCI was performed using an electron energy of 70 eV and an emission current of 250 μA . The source temperature employed for all ionization techniques was 200 $^\circ\text{C}$.

Analyses of pentane extracts of polysulfide solutions (in some cases following methylation) were conducted via GC/MS (EI mode), using a cold on-column injector to minimize the potential for desulfurization reactions. Separations were effected using the DB-200 capillary column previously described.

Results

Kinetics of Atrazine Reaction with Polysulfides. Initial experiments focused on the kinetics of atrazine reaction with polysulfides. Solutions were prepared by reacting HS^- with excess S_8 to form polysulfide dianions according to a pH-dependent reversible reaction (28–30)



Additional solutions were prepared by dissolving purified $\text{Na}_2\text{S}_4(\text{s})$ at pH 9. Dissolution of Na_2S_4 at pH 9 was ac-

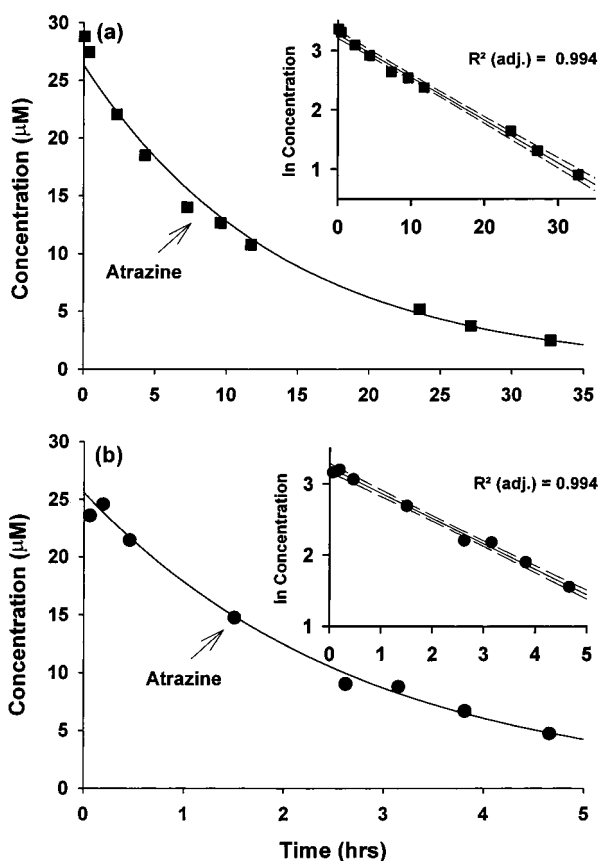


FIGURE 1. Atrazine (27 μM) reaction with (a) a polysulfide solution containing 3.9 mM $\Sigma[\text{S}_n^{2-}]$ and (b) a polysulfide solution containing 18.6 mM $\Sigma[\text{S}_n^{2-}]$. Both solutions contain 0.18 M NaCl/0.04 M borate buffer (pH 9.0–9.1) at an ionic strength of 0.24 equiv/L. Both experiments were conducted at 25.0 $^\circ\text{C}$. Solid lines represent the exponential fits to the data. Insets depict the same data plotted in semilogarithmic form. The dashed lines in the insets represent the 95% confidence limits to the regressions.

companied by a near-instantaneous development of turbidity, interpreted as evidence of elemental sulfur precipitation (and hence, disproportionation of S_4^{2-}). For the Na_2S_4 solutions at pH 9, $\Sigma[\text{S}_n^{2-}]$ was hence computed from measured $[\text{S}(0)]_{\text{poly}}$, assuming that the relative concentrations of S_n^{2-} and HS_n^- species are as dictated by equilibrium considerations. Note that HS^- was estimated to comprise as much as 56% of the $[\text{S}(-\text{II})]_{\text{T}}$ under this assumption.

Example time courses obtained at two different $\Sigma[\text{S}_n^{2-}]$ values are presented in Figure 1. The slope of a semilogarithmic plot yields a pseudo-first-order rate constant k_{obs} ; the high degree of linearity over two half-lives is indicative of a first-order dependence on atrazine concentration.

Figure 2a summarizes the data obtained at pH 9 and varying $\Sigma[\text{S}_n^{2-}]$ for polysulfide solutions prepared in both fashions described. Details of solution composition and rate constants for each experiment with atrazine are provided in the Supporting Information (Table S1). The order of the reaction with respect to $\Sigma[\text{S}_n^{2-}]$ in each case was determined by regressing $\log k_{\text{obs}}$ versus $\log \Sigma[\text{S}_n^{2-}]$. The slopes were found to be equal to 1.12 ± 0.17 for solutions prepared by equilibrating HS^- with S_8 and 0.96 ± 0.18 for solutions prepared with $\text{Na}_2\text{S}_4(\text{s})$, where uncertainties reflect 95% confidence limits. This indicates that the reactions are essentially first-order in $\Sigma[\text{S}_n^{2-}]$. The data were thus reanalyzed by regressing k_{obs} against $\Sigma[\text{S}_n^{2-}]$. The intercepts of the fits were not significantly different from zero (at the 95% confidence level) in each case, signifying that other species present in solution (e.g., borate, hydroxide) do not react with

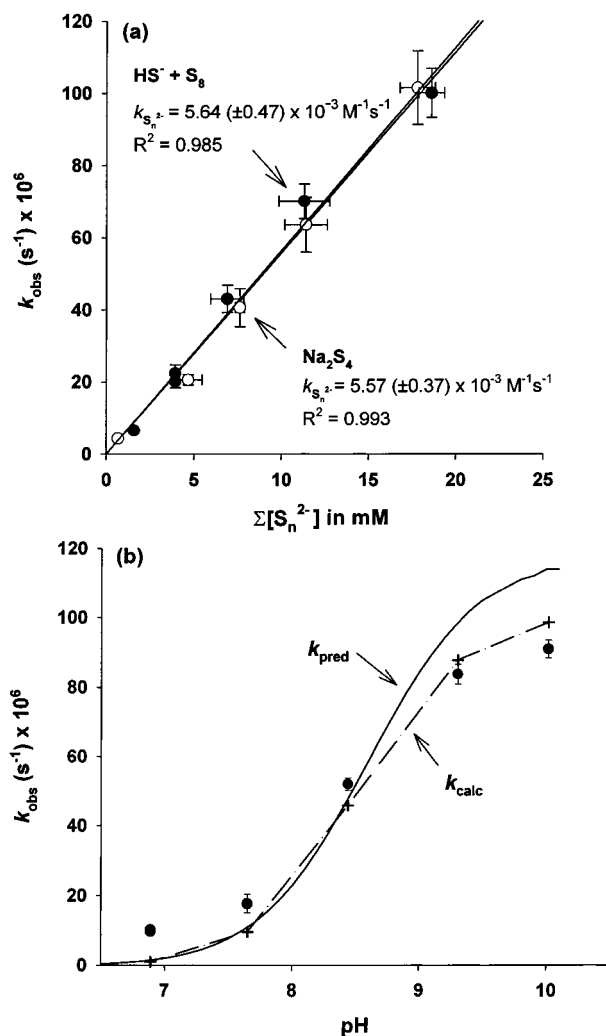


FIGURE 2. (a) Plot of pseudo-first-order rate constants k_{obs} (s^{-1}) versus polysulfide concentrations $\Sigma[S_n^{2-}]$ for reactions of atrazine at pH 9 with polysulfide solutions prepared in two different ways: via equilibration of HS^- with S_8 (●) and via dissolution of purified $\text{Na}_2\text{S}_4(\text{s})$ (○). Solid lines represent linear regressions with intercepts forced to zero. (b) Plot of experimental pseudo-first-order rate constants k_{obs} (●) versus solution pH for reaction of atrazine with polysulfides. Solid line represents the pseudo-first-order rate constant k_{pred} predicted from a second-order rate constant $k_{\text{S}_8^{2-}}$ of $5.64 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$ and polysulfide concentrations predicted from equilibrium between HS^- and S_8 . Dashed line with crosshairs at each solution point (+) represents the pseudo-first-order rate constant k_{calc} anticipated in each experiment from $k_{\text{S}_8^{2-}}$ and $\Sigma[S_n^{2-}]$ inferred from measured $[\text{S}(0)]_{\text{poly}}$ and pH. Note that the minimum experimentally accessible pseudo-first-order rate constant under these conditions is approximately 10^{-7} s^{-1} and that no discernible atrazine transformation was observed in complementary buffer control experiments spanning this pH range.

atrazine at appreciable rates under the conditions employed. Indeed, rates of atrazine reaction were found to be negligible ($k_{\text{obs}} < 1 \times 10^{-7} \text{ s}^{-1}$) in control experiments conducted at this pH in borate buffer or in bisulfide solutions at relatively high $[\text{HS}^-]$ (5–37 mM) over periods as long as 6 days. This lack of reaction in bisulfide solutions implies that S^{2-} is present at too low a concentration in these experiments to serve as a reactive species.

Second-order rate constants $k_{\text{S}_n^{2-}}$ were determined by conducting regressions with the intercepts forced to zero, as shown in Figure 2a. This is equivalent to computing second-order rate constants by dividing each k_{obs} value by the appropriate $\Sigma[S_n^{2-}]$ value and then averaging the results for

each type of solution. Note that $k_{\text{S}_n^{2-}}$ represents an effective second-order rate constant, equivalent to $\sum_{j=2}^5 k_{\text{S}_j^{2-}} \alpha_j$, where $k_{\text{S}_j^{2-}}$ is a second-order rate constant for each individual polysulfide dianion and α_j is the fraction of $\Sigma[S_n^{2-}]$ present as each dianion. The value of $k_{\text{S}_n^{2-}}$ computed from the solutions prepared by equilibrating HS^- with S_8 is not significantly different from that obtained in solutions prepared with $\text{Na}_2\text{S}_4(\text{s})$. Values were $(5.64 \pm 0.47) \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$ and $(5.57 \pm 0.37) \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$, respectively.

The close correspondence of estimates of $k_{\text{S}_n^{2-}}$ might be interpreted as additional evidence that disproportionation of the S_4^{2-} in the Na_2S_4 solution had occurred, producing a mixture of polysulfides identical to that obtained on equilibrating HS^- with S_8 . The principal polysulfide anticipated in such a mixture, however, is S_4^{2-} , with S_5^{2-} present at 76% of the S_4^{2-} concentration and other polysulfide dianions present at much lower concentrations (see Supporting Information, Figure S1). Similar $k_{\text{S}_n^{2-}}$ values could equally well signify that one or more of the other polysulfides present in an HS^-/S_8 mixture is more reactive than S_4^{2-} .

Qualitative identification of polysulfides in the two solutions at pH 9 was accomplished via methylation with CH_3I , followed by extraction into pentane and analysis via GC/MS. Results yielded a similar distribution of dimethyl polysulfides (with 2–6 sulfur atoms), in which dimethyl-trisulfide was the most abundant species. This contrasts with results obtained in a methylated Na_2S_4 solution prepared without buffer (pH > 12); although the same dimethyl polysulfides were observed, their relative abundances were quite different, with dimethyl tetrasulfide being present at highest concentration. Nor did the Na_2S_4 solution at the higher pH develop the turbidity noted at pH 9. Moreover, no S_8 was detected in analysis (via GC/MS) of a pentane extract of an unmethylated Na_2S_4 solution at high pH, while a significant S_8 peak was obtained in a comparable analysis for an Na_2S_4 solution at pH 9. Together with the similarity in $k_{\text{S}_n^{2-}}$, the results support the hypothesis that the S_4^{2-} in the Na_2S_4 solution at pH 9 undergoes disproportionation to an equilibrium mixture of polysulfides, S_8 , and HS^- (reverse of eq 1).

It should be noted that the distribution of dimethyl polysulfides obtained on methylation may not reflect their equilibrium distribution prior to reaction with CH_3I . For example, alkylated polysulfides have been reported to undergo desulfurization in the presence of nucleophiles (31). Species such as HS^- , S_n^{2-} , or RS_n^- present in solution could attack derivatized polysulfides, reducing the length of the sulfur chain.

On the basis of published stability constants for polysulfides and hydropolysulfides, appreciable quantities of the latter can be anticipated at neutral pH, as shown by the equilibrium speciation diagram given in the Supporting Information (Figure S1). To test whether hydropolysulfides could play a role in the observed transformation of atrazine, experiments were conducted with polysulfide solutions at constant $[\text{S}(-\text{II})]_{\text{T}}$ over a pH range of 6.9–10.2. Results are shown in Figure 2b.

As anticipated, the pseudo-first-order rate constant k_{obs} for reaction in the presence of polysulfides increases with pH as the position of eq 1 shifts to the right and higher concentrations of polysulfides form (see Figure S1). Some discrepancies were observed, however, between experimental k_{obs} and pseudo-first-order rate constants that might be predicted from existing models of polysulfide speciation. The solid line in Figure 2b represents the pseudo-first-order rate constant k_{pred} that might be anticipated from the second-order rate constant determined at pH 9 ($5.64 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$) and literature-derived polysulfide stability constants (28–30). For the highest pH values tested, reaction rates predicted in this fashion are greater than the measured rates.

This may reflect errors in stability constants or a lack of polysulfide equilibrium in our solutions; note that contributions from reactions with OH⁻ (20), H₂O, or H⁺ (32) are negligible at these pH values. Pseudo-first-order rate constants k_{calc} were therefore also computed by multiplying the second-order rate constant by the calculated $\Sigma[S_n^{2-}]$ inferred from measured $[S(0)]_{\text{poly}}$. Results are shown via the dashed line with crosshairs (+) in Figure 2b. These values correspond quite well to experimental k_{obs} at higher pH.

Experimental k_{obs} values are substantially higher than predicted values at pH < 8. Discrepancies between experimental k_{obs} and k_{pred} or k_{calc} could potentially indicate that HS_n⁻ species contribute appreciably to the rate of atrazine reaction. Efforts to compute a second-order rate constant for HS_n⁻ through multiple regression analyses of an expression of the form $k_{\text{obs}} = k_{S_n^{2-}} \cdot \Sigma[S_n^{2-}] + k_{HS_n^-} \cdot \Sigma[HS_n^-]$ resulted in estimates of $k_{S_n^{2-}} = (5.10 \pm 0.21) \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$ and $k_{HS_n^-}$ of $(0.27 \pm 0.02) \text{ M}^{-1} \text{ s}^{-1}$. That $k_{HS_n^-}$ should be substantially greater than $k_{S_n^{2-}}$ is counter to the trends anticipated for nucleophilic reactivity. Uncertainties in pK_a values for hydropolysulfides are unlikely to be of sufficient magnitude as to explain the results. This may suggest that HS_n⁻ reacts via a different mechanism, perhaps as a general acid catalyst. The value of $k_{HS_n^-}$ we compute is, however, far greater than $k_{H_2PO_4^-}$ reported (32) for general acid catalysis of atrazine hydrolysis of $5.6 \times 10^{-9} \text{ M}^{-1} \text{ s}^{-1}$, even though HS_n⁻ and H₂PO₄⁻ possess comparable acidity. Unfortunately, hydroxyatrazine (the anticipated product of general acid-catalyzed hydrolysis) would not be detected by the analytical methods employed. No reaction of atrazine could be discerned in two control experiments conducted with two other sulfur nucleophiles (thiosulfate and sulfite; 50 mM) that could conceivably be present in polysulfide solutions.

Atrazine Reaction Products. Atrazine reacts with polysulfides to form a sulfur-substituted triazine product, as identified by derivatization of spent reaction mixtures with CH₃I or PFBBBr. The PFB atrazine derivative was characterized by GC/MS (EI/PCI/NCI). The mass spectra are consistent with a product containing only a single sulfur atom bound to the triazine ring (Figure 3). The EI spectrum indicates a significant molecular ion M⁺ at m/z 393, and the PCI spectrum is consistent with this structure, exhibiting both the protonated (M + H)⁺ ion and an adduct (M + C₂H₅)⁺ of the molecular ion. The NCI spectrum does not demonstrate the formation of a negatively charged molecular ion M⁻, but does yield an intense sulfur-substituted triazine fragment (M - PFB)⁻ at m/z 212. This type of fragmentation is characteristic of NCI spectra of PFB derivatives of carboxylic acids (33), in which the parent ion is rarely observed. Identification of the sulfur-substituted product resulting from atrazine reaction with polysulfides was further confirmed by methylation with CH₃I. Both the mass spectrum (EI) and the retention time of the methylated product were identical to that of authentic (2-ethylamino)-4-(isopropylamino)-6-(methylthio)-s-triazine (commonly known as the herbicide ametryn). Yields of ametryn ranged between 95% and 103%.

None of the azine reaction products identified herein contained disulfide or higher polysulfide linkages. The absence of the multiple sulfur atoms anticipated in a product resulting from substitution of halogen by a polysulfide dianion may indicate desulfurization of the polysulfide linkage. A polysulfide chain bound to the electron-withdrawing triazine ring of atrazine may be subject to nucleophilic attack by desulfurizing agents (e.g., HS⁻, S_n²⁻, CH₃S⁻ formed by reaction of CH₃I with HS⁻) through attack at a sulfur atom in the polysulfide chain. Polysulfide chains attached to electronegative groups (e.g., aryl) tend to donate electrons from one sulfur atom to another to increase resonance stability, increasing their susceptibility to nucleophilic attack. In fact, the longest chain length observed for polysulfides bound to

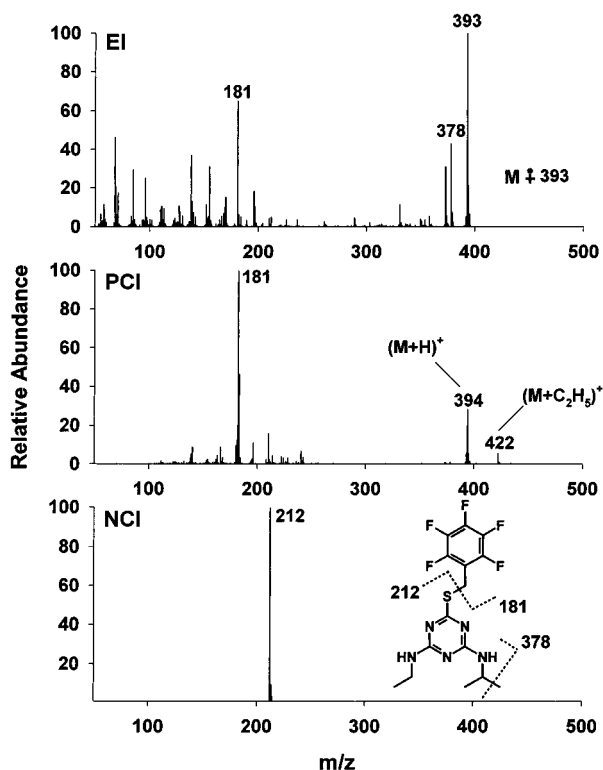


FIGURE 3. Mass spectra (EI, PCI, and NCI) of product (with retention time (rt) of 24.7 min) obtained from reaction of atrazine with polysulfides (following pentafluorobenzoylation). The rt for atrazine under these conditions is 13.86 min.

tert-alkyl, primary alkyl, and aryl substituents (increasing in electron-withdrawing capability) in the presence of ammonium sulfide were tetra-, tri-, and disulfide, respectively (34). Similarly, only mono- and disulfide products were obtained in the S_NAr reactions of nitroaromatic halides with electrogenerated polysulfides (S₆²⁻ and S₈²⁻) in dimethylacetamide (35).







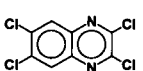
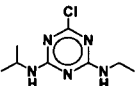
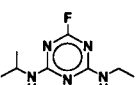
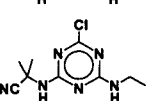
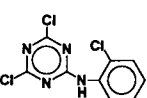
Cyanazine Reaction with Bisulfide and Polysulfides.

Cyanazine readily reacts with polysulfides (see Table 1), with reactivity comparable to that of atrazine. In contrast to the behavior of atrazine, cyanazine did react slowly with HS⁻ (85% decay over a 2 day period in 11.8 mM HS⁻ solution at pH 8.1). No reaction was observed in the corresponding phosphate buffer control at pH 8.1. A longer-term (1 month) experiment was conducted at pH 7 to obtain a second-order rate constant (Table 1) for reaction of cyanazine with HS⁻, with comparable results. The close comparison of computed $k_{S_n^{2-}}$ values (assuming HS⁻ is the sole reactive species) indicates that S₂²⁻ is present at too low a concentration to contribute appreciably to reaction of cyanazine. In computing $k_{S_n^{2-}}$ for cyanazine, k_{obs} obtained in the presence of polysulfides was corrected to account for concurrent reaction with HS⁻. The mass spectrum of the methylated cyanazine product was consistent with that anticipated for 2-(4-thiomethyl-6-(ethylamino)-s-triazin-2-yl)amino-2-methylpropionitrile (cyanatryn) (Figure S2, Supporting Information). Owing to a lack of authentic reference materials, we were unable to determine the yield of this product. No evidence of any nitrile hydrolysis product was obtained (25).

Anilazine Reaction with Bisulfide and Polysulfides. This chloroazine is considerably more reactive than is atrazine and reacts at appreciable rates with both HS⁻ and S_n²⁻. Corrections were therefore made for the contribution of HS⁻ in computing $k_{S_n^{2-}}$. This contribution amounted to 0.04% of k_{obs} measured in a bisulfide/polysulfide mixture.

Anilazine reacts with HS⁻ and S_n²⁻ to yield two transformation products, which were characterized by methylation

TABLE 1. Second-order Rate Constants for Reactions of Bisulfide and Polysulfides with Selected Chloro- (and Fluoro)Azine Compounds at 25.0 °C^a

Azine	Structure	Abbrev	k_{HS^-} (M ⁻¹ s ⁻¹) ^b	$k_{\text{S}_n^{2-}}$ (M ⁻¹ s ⁻¹) ^b	$k_{\text{S}_n^{2-}}/k_{\text{HS}^-}$
<i>Chlorinated Pyridine:</i>					
2,6-dichloropyridine		DCP	not reactive	4.1(± 2.3)×10 ⁻⁵	na ^c
<i>Chlorinated Pyrimidines:</i>					
2-amino-4,6-dichloropyrimidine		ADCPm	4.43(± 0.98)×10 ⁻⁵	6.15(± 0.92)×10 ⁻²	1,400
2-chloropyrimidine		CPm	not reactive	4.46(± 0.52)×10 ⁻⁴	na ^c
4,6-dichloropyrimidine		DCPm	3.17(± 0.21)×10 ⁻⁴	1.06(± 0.13)	3,300
2,4,5,6-tetrachloropyrimidine		TCPm	1.25(± 0.06)	> 350 ^d	> 280
<i>Chlorinated Quinoxalines:</i>					
2,3-dichloroquinoxaline		DCQ	3.56(± 0.33)×10 ⁻³	1.62(± 0.14)	460
2,3,6,7-tetrachloroquinoxaline		TCQ	1.18(± 0.11)×10 ⁻²	37(± 71) ^e	3,100
<i>Halogenated Triazines:</i>					
Atrazine		Atraz	not reactive	5.64(± 0.47)×10 ^{-3 f}	na ^c
Fluoroatrazine		Fatrz	not reactive	3.99(± 0.42)×10 ⁻³	na ^c
Cyanazine		Cyaz	9.21(± 2.0)×10 ^{-5 g}	6.90(± 0.62)×10 ⁻³	75
Anilazine		Anlz	2.73(± 0.27)×10 ⁻¹	3.04(± 1.38)×10 ²	1,100

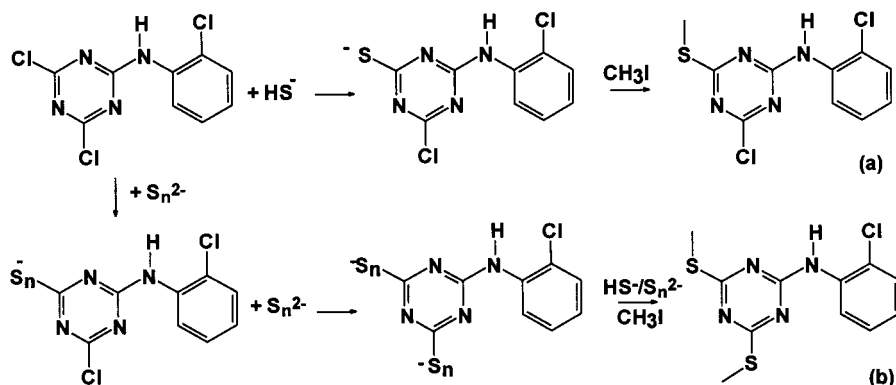
^a Unless indicated otherwise, all rate constants were determined at pH 8.9–9.1 (20 mM borate buffer for HS⁻ experiments, 40 mM borate buffer for S_n²⁻ experiments) and ionic strength = 0.24 equiv/L (adjusted with NaCl). ^b Uncertainties represent 95% confidence limits. Computed k_{HS^-} values neglect potential contribution from S²⁻. ^c na = not available; no observable reaction of chloroazine with HS⁻. ^d Minimum estimate of rate constant ($t_{1/2} < 10$ s in the presence of 90 μM Σ[S_n²⁻]). ^e Estimated rate constant; conditions may not have been pseudo-first-order since Σ[S_n²⁻]/[TCQ] only ~10. ^f Obtained from Figure 2 (HS⁻ + S₈ solutions). ^g An average of two experiments at pH 7.0 and 8.1 (0.5 mM phosphate buffer) and ionic strength = 0.4 equiv/L (adjusted with NaCl). Note that reaction may occur in part through nucleophilic attack at nitrile substituent.

with CH₃I, followed by GC/MS (EI) analysis (Scheme 2). Bisulfide reacts with anilazine via the displacement of a single chlorine to yield a monochloro-monosulfur substituted (1-Cl, 1-S) triazine product (product a). Polysulfides, in contrast, are able to displace both of the chlorines on the triazine ring to generate a disulfur substituted (2-S) triazine (product b) as the major product. The mass spectra are provided in the Supporting Information (Figure S3).

Reactions of Other Haloazines. To complement the studies conducted with chloro-*s*-triazines, reactions of HS⁻ and S_n²⁻ with a group of halogenated pyridine, pyrimidine and quinoxaline compounds, in addition to a fluorinated analogue of atrazine, were investigated. These experiments were designed to discern the influence of aza nitrogens, as

well as halogen and amino substituents, on the reactivity of haloazines with reduced sulfur nucleophiles. Second-order rate constants are summarized in Table 1; these were estimated by dividing the pseudo-first-order rate constants measured for each haloazine by the concentration of the relevant reduced sulfur species [HS⁻] or Σ[S_n²⁻] (with the latter computed from measured [S(0)_{poly}]). In the cases where haloazines reacted with both HS⁻ and S_n²⁻, the pseudo-first-order rate constant was first corrected to account for the contribution of HS⁻. This was accomplished by using the second-order rate constant for HS⁻ measured in the absence of polysulfides, in conjunction with the computed [HS⁻] present. Detailed experimental data are provided elsewhere (25).

SCHEME 2



It should be noted that most $k_{\text{S}_n^{2-}}/k_{\text{HS}^-}$ ratios in Table 1 are substantially greater than previously reported (13, 14) for $\text{S}_\text{N}2$ reactions of alkyl halides. This raises the possibility that trace polysulfides present in our bisulfide solutions could contribute to the observed reaction rates, leading to overestimation of k_{HS^-} . The lowest measurable polysulfide concentration in our "polysulfide-free" bisulfide solutions (10 mM HS^-) was $0.03 \mu\text{M} \sum [\text{S}_n^{2-}]$ (as determined from a $0.1 \mu\text{M}$ method detection limit for $[\text{S}(0)]_{\text{poly}}$). Measured polysulfide concentrations never exceeded this detection limit. If we assume that $k_{\text{S}_n^{2-}}/k_{\text{HS}^-}$ for DCPm is 3300, this trace polysulfide contaminant could only account for 1% of k_{obs} . For the other azines listed in Table 1, for which $k_{\text{S}_n^{2-}}/k_{\text{HS}^-}$ is smaller (ranging from 75 to 3100), the potential contribution of trace polysulfides to k_{obs} is even less. Although we cannot rule out the possible presence of trace polysulfides in the polysulfide-free solutions, they are unlikely to affect the k_{HS^-} values reported in Table 1.

Reaction Products of Other Haloazines. Products inferred (via mass spectral interpretation) for haloazine reactions with reduced sulfur nucleophiles are indicated in Table S2 in the Supporting Information. In general, HS^- was able to displace all but one chlorine from the chloroazines investigated. Trace quantities of the fully substituted azine products were observed in the case of reactions of DCQ and TCQ with HS^- . Polysulfides evinced a substantially greater ability to displace all of the halogens from the azines, with the exception of 2,6-dichloropyridine (DCP) and tetrachloropyrimidine (TCPm). In the former case, only one chlorine of DCP was displaced to form the monochlorine-monosulfur pyridine product. This product contains only one aza nitrogen and one chlorine substituent and is, thus, relatively unactivated to further reaction with polysulfides. For TCPm, it is possible that the reaction largely ceased after the third substitution step because polysulfides became depleted in solution at the low ratios of polysulfide to TCPm employed. Analysis of the product of 2-chloropyrimidine (CPm) reaction with polysulfides demonstrates that incorporation of a second aza nitrogen in the ring allows even a single chlorine to be displaced from a pyrimidine.

Discussion

The rate constants provided in Table 1 reveal a wide range of reactivity of chloroazines toward HS^- and S_n^{2-} . In general, a greater number of chlorine substituents confers enhanced $\text{S}_\text{N}2$ reactivity. Moreover, additional ring aza nitrogens, as well as the presence of a fused ring system (bicyclic heterocycles), tend to result in increased reactivity. Subtle variations in azine structure can influence the stability of the σ complex, as can changes in the identity of the nucleophile. These, in turn, affect the energy barrier associated with the rate-determining step and, hence, the rate of the overall reaction. Differences in reactivity can largely be rationalized

by examining the structural features controlling the initial rate of nucleophilic attack.

Influence of Aza Nitrogens on Reactivity. Using atrazine as an example, it is apparent that ring aza nitrogens present α and γ to the site of chlorine substitution help stabilize the negative charge of the σ complex via mesomeric effects (Scheme 1). Nitrogen is more electronegative than carbon; these aza nitrogens, therefore, also contribute an inductive effect that increases the susceptibility of the carbon to nucleophilic attack. The influence of aza nitrogens through such effects has previously been demonstrated in a systematic study of chloropyridine and chlorobenzene reactions with methoxide ion in methanol by Miller and co-workers (36, 37). In these studies, chloropyridines with the aza nitrogen at α and γ positions were observed to be significantly more reactive than chlorobenzene toward the displacement of chlorine, with the γ position slightly more reactive (2.8×10^8 -fold and 7.4×10^9 -fold increase in $k_{\text{CH}_3\text{O}^-}$ for 2-chloropyridine and 4-chloropyridine, respectively, relative to $k_{\text{CH}_3\text{O}^-}$ for chlorobenzene). That the effect of the ring aza nitrogen on reactivity stems in part from inductive effects is demonstrated by 3-chloropyridine, which is 9.1×10^4 -fold more reactive than chlorobenzene toward methoxide (36).

The effect of aza nitrogens on reactivity is exemplified in this study by comparing DCP to DCPm. DCPm, containing two aza nitrogens (at α and γ positions), is $\sim 10^4$ -fold more reactive toward S_n^{2-} than is DCP, with only one aza nitrogen (α to either possible site of nucleophilic attack). This rate enhancement is primarily attributable to the inductive and mesomeric influences of the additional aza nitrogen, although the γ position of the aza nitrogens of DCPm no doubt also contributes to the enhanced reactivity. Note that we found 1,2,4,5-tetrachlorobenzene (containing four chlorine substituents but no aza nitrogens) to be unreactive with S_n^{2-} under our experimental conditions.

Substituent Effects. The effect of the number of chlorine substituents (and their position on the azine ring) can be demonstrated by comparing the chlorinated pyrimidines. Here, a reactivity trend of TCPm > DCPm > CPm is observed for both HS^- and S_n^{2-} . A 10^3 -fold increase in reactivity toward S_n^{2-} is observed for DCPm versus CPm. This stems from the combined influence of a second electron-withdrawing chlorine substituent and its more reactive γ position.

Anilazine is $>10^4$ -fold more reactive than is atrazine toward polysulfides. Reactivity contrasts have also been observed in the hydrolysis of these two agrochemicals; anilazine has been reported to liberate chloride ion under slightly alkaline conditions (38), whereas atrazine is relatively stable to hydrolysis at moderate pH (39). One difference between anilazine and atrazine is that the electron-donating alkylamino group ($-\text{NHR}$) of atrazine has been replaced by an electron-withdrawing chlorine substituent. Differences

in substituent inductive effects are largely responsible for the observed differences in reactivity.

Anilazine also contains an *o*-chloroanilino group, in place of the second alkylamino substituent of atrazine. The replacement of a moderately electron-donating alkylamino group by a slightly less electron-donating anilino group should contribute to a much lesser extent to the observed differences in reactivity between atrazine and anilazine (25).

Comparison of the rate constants for reaction of DCPm and ADCPm with HS^- and S_n^{2-} illustrates the effect of substituting an electron-donating amino group for hydrogen. The presence of the 2-amino substituent α to the ring aza nitrogens results in a 7–17-fold decrease in reactivity toward HS^- and S_n^{2-} , respectively.

Influence of Fused Ring Systems. DCQ proved to be 11-fold more reactive than DCPm toward HS^- . For reactions of DCQ and DCPm with S_n^{2-} , a rate enhancement of 1.5-fold was observed on adding a second fused ring. These reactivity enhancements can be attributed to delocalization of the developing charge of the σ complex throughout the extended aromatic system. Chapman and Russell-Hill (40) have noted modest rate enhancements (5-fold) in fused systems in comparing the reactivity of 2-chloroquinoxaline and 2-chloropyrimidine with the ethoxide ion in ethanol. Greater reactivity contrasts might be anticipated for compounds with comparable substitution patterns (e.g., DCQ versus 2,3-dichloropyrazine).

Leaving Group Effects. The identity of the nucleofuge greatly influences the reactivity of alkyl halides in nucleophilic displacement reactions. In particular, the strength of the bond to the leaving group affects $\text{S}_\text{N}1$ and $\text{S}_\text{N}2$ reactivity because bond-breaking occurs during the rate-determining step. The first step in $\text{S}_\text{N}2$ reactions, involving the addition of the nucleophile, is typically rate-determining rather than the step involving expulsion of the leaving group, and even compounds possessing what are normally viewed as poor leaving groups can be good $\text{S}_\text{N}2$ substrates. In fact, a reactivity trend of $\text{F} > \text{Cl} > \text{Br} > \text{I}$ has been reported for the displacement of halogen in *p*-halonitrobenzenes by methoxide (41), reflecting the ability of strong electron-withdrawing substituents to stabilize the transition state leading to the σ complex. For this reason, many fiber-reactive dyes contain fluorine as a nucleofuge.

Atrazine was observed to be 1.4-fold more reactive than its fluorinated analogue toward S_n^{2-} . Even though the relative reactivity trend was opposite to that previously observed for *p*-halonitrobenzenes, fluoride still should be considered as a potential leaving group in environmental $\text{S}_\text{N}2$ reactions. Differences in relative reactivity between S_n^{2-} and CH_3O^- as the nucleofuge is varied may stem from less favorable “hard–soft” interactions (42) between the highly polarizable nucleophile S_n^{2-} and the “hard” leaving group F^- . It has been suggested (42) that electron repulsion within the σ complex is reduced if the leaving group and the nucleophile are of similar polarizability, thereby facilitating σ bond formation.

Relative Reactivity of S_n^{2-} versus HS^- . In all cases, azines displayed much greater reactivity toward S_n^{2-} than toward HS^- , the ratio $k_{\text{S}_n^{2-}}/k_{\text{HS}^-}$ having varied from 75 to 3300 (Table 1). Within an individual class of azines, this ratio tended to increase with increasing chlorination, with the greatest value observed for TCQ. The reactivity contrasts ($k_{\text{S}_n^{2-}}/k_{\text{HS}^-}$) for haloazines are greater than observed for $\text{S}_\text{N}2$ reactions of chloroacetanilides (25, 43) and other alkyl halides ($k_{\text{S}_n^{2-}}/k_{\text{HS}^-}$ of 45 for 1-chlorohexane; see ref 25). Smaller ratios have also been reported for nucleophilic (Michael) addition to acrylic acid and acrylonitrile ($k_{\text{S}_n^{2-}}/k_{\text{HS}^-}$ of 28 and 5, respectively; see ref 44).

The high reactivity of S_n^{2-} relative to HS^- might appear counterintuitive because HS^- is a slightly stronger base ($\text{p}K_\text{a}$ of H_2S is 6.98 (see ref 26), while $\text{p}K_\text{a}$ values of HS_4^{2-} and HS_5^{2-}

are 6.1–6.7 (see ref 28)). Differences in charge and size between the two nucleophiles may also contribute to differences in reactivity. Polysulfides have an overall charge of -2 , which can be distributed over several sulfur atoms (45) via delocalization into d orbitals (46). In contrast, HS^- has a localized charge of -1 and may, hence, be more highly solvated despite its lower overall charge than a bulkier, more diffusely charged polysulfide dianion.

The high reactivity of S_n^{2-} relative to HS^- for azines may stem in part from the α effect, in which nucleophiles possessing lone pairs on an atom adjacent to the attacking atom exhibit anomalously high nucleophilicity, particularly for substitution at unsaturated carbon. This α effect has been extensively discussed (47, 48) and has been attributed to reduced solvation of the nucleophile or to an increase in the ground-state energy caused by lone pair electron repulsion. A recent investigation (49) has provided evidence of ground-state desolvation of an α nucleophile in mixed aqueous/organic solvent (50/50 $\text{H}_2\text{O}/\text{DMSO}$) in the nucleophilic acyl substitution reaction of *p*-nitrophenyl acetate with butane-2,3-dione monoximate.

If, in fact, repulsion between adjacent electron pairs contributes to increased nucleophilicity, one would predict S_2^{2-} , S_3^{2-} , S_4^{2-} , S_5^{2-} , and S_6^{2-} to have markedly different ground-state energies and, hence, different reactivities. Previously summarized (50) energies of the highest occupied molecular orbital (E_{HOMO}) of S_3^{2-} (-4.66 eV) and S_4^{2-} ($+1.36$ eV) confirm a large difference in ground-state energies of these two nucleophiles; other factors being equal, more negative E_{HOMO} indicates an increase in stability and hence a decrease in nucleophilic reactivity. Variations in E_{HOMO} have been invoked to rationalize the increased reactivity of S_4^{2-} , relative to HS^- ($E_{\text{HOMO}} = -2.5$ eV), toward activated olefins (51). Differences in reactivity between polysulfide dianions would be difficult to demonstrate in our experimental systems if (as we suspect) polysulfides rapidly disproportionate to an equilibrium mixture in water.

Structure–Activity Relationships (SARs). Attempts were made to develop SARs that could be used to predict the reactivity of untested azines with HS^- or S_n^{2-} . In so doing, we selected the energy of the lowest unoccupied molecular orbital (E_{LUMO}) as a predictor of different substrates' susceptibility to nucleophilic attack. E_{LUMO} values were calculated using a semiempirical molecular orbital method (AM1) with a solvation model for water (SM2, C–T water solvation; see ref 52). The relative electron deficiencies of the aromatic substrates, resulting from inductive and mesomeric interactions with ring aza nitrogens and substituents attached to the aromatic ring, would be expected to be manifested by differences in E_{LUMO} values. Note that this simplistic approach relegates all differences in reactivity of chloroazines to variations in their electrophilicity; steric effects and hard/soft interactions between the nucleophile and the leaving group in the transition state are ignored.

Plots of second-order rate constants $k_{\text{S}_n^{2-}}$ and k_{HS^-} for chloroazines as a function of E_{LUMO} are shown in Figure 4. The results, although displaying considerable scatter, do display the anticipated *general* trend of increasing azine reactivity with decreasing E_{LUMO} . This is true for both HS^- and S_n^{2-} . Upon close examination of the data, the scatter diminishes somewhat within individual classes of azines. This is demonstrated best for the largest data sets, involving reactions of pyrimidines (\square) with HS^- and for reactions of triazines (\blacktriangle) with S_n^{2-} . This illustrates the general point that E_{LUMO} energies may not be consistent between different classes of compounds. Burrow et al. (53) have similarly noted that E_{LUMO} may prove valid as a predictor for rates of reaction of zerovalent iron within, but not between, groups of chloroalkanes and chloroalkenes. This point is further demonstrated by the substantial contrasts in $k_{\text{S}_n^{2-}}$ for

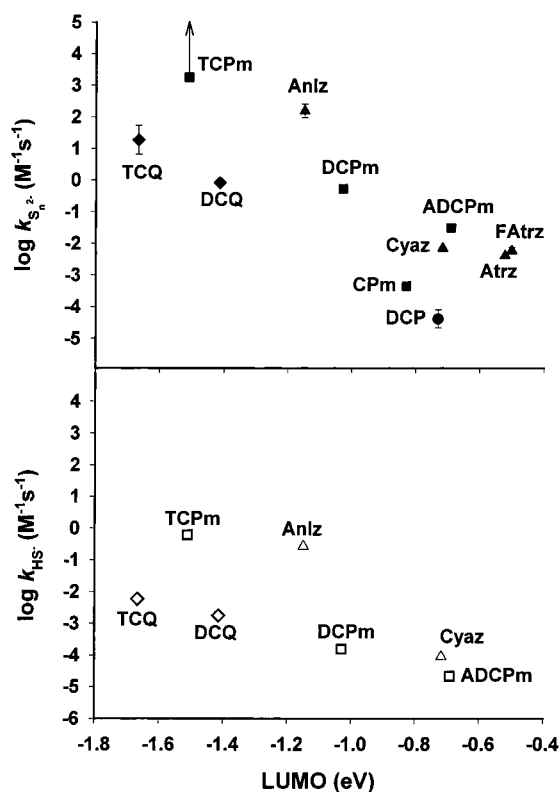


FIGURE 4. Correlation of second-order rate constants for reactions of chloroazines with sulfur nucleophiles as a function of calculated AM1–SM2 (C–T water solvation) E_{LUMO} (eV). Chloroazine classes are identified with different symbols (● pyridine, ■ pyrimidine, ◆ quinoxaline, and ▲ triazine). Note that because of the highly reactive nature of TCPm with S_n^{2-} , the rate constant provided represents a minimum estimate ($t_{1/2} < 10$ s; see Table 1), as indicated by the upward arrow. Note also that a statistical factor of 2 was applied in plotting second-order rate constants for DCP, ADCPm, DCPm, TCPm, DCQ, TCQ, and Anlz.

ADCPm, Cyaz, and DCP, despite comparable E_{LUMO} values.

It is apparent that caution should be exercised in attempting to develop models to predict chemical reactivity that are based on descriptors as simple as E_{LUMO} values. A more rigorous (yet considerably more demanding) approach to developing SARs for S_nAr reactions might be to include energies of the σ complex (or possibly the transition-state structure leading to this intermediate) relative to the energy of the starting materials; such computations should include solvation effects. Theoretical *ab initio* and semiempirical studies of σ complexes and related transition states have been previously employed to explore factors governing the regioselectivity of halonitrobenzenes in S_nAr reactions (54), as well as to locate the minimum energy pathway in chloronitrobenzene reactions with a range of nucleophiles in the gas phase (55).

Environmental Significance of Chloroazine Reactions with Sulfur Nucleophiles. Polysulfides are extremely reactive nucleophiles that could potentially control the environmental fate of chloroazine agrochemicals and fiber-reactive dyes within hypoxic coastal marine sediment porewaters. In particular, the results of this study demonstrate that chloroazines are much more reactive toward polysulfides than toward HS^- .

We can use the rate constants shown in Table 1 to predict the persistence of chloroazines under environmentally relevant conditions. Half-lives for azines in marine porewaters containing reduced sulfur species were predicted by multiplying second-order rate constants by the concentrations

TABLE 2. Predicted Half-Lives of Chloro (and Fluoro)azines in a Salt-Marsh Sediment Porewater at pH 7.2 Containing 3.4 mM $[\text{HS}^-]$ and 0.33 mM $\Sigma[\text{S}_n^{2-}]^{a,b}$

azine	abbrev	half-life ($t_{1/2}$) ^c	% of reaction attributable to S_n^{2-} ^d
Chlorinated Pyridine			
2,6-dichloropyridine	DCP	592 days	100
Chlorinated Pyrimidines			
2-amino-4,6-dichloropyrimidine	ADCPm	0.4 days	99
2-chloropyrimidine	CPm	54 days	100
4,6-dichloropyrimidine	DCPm	33 min	100
2,4,5,6-tetrachloropyrimidine	TCPm	<1 min	97
Chlorinated Quinoxalines			
2,3-dichloroquinoxaline	DCQ	21 min	98
2,3,6,7-tetrachloroquinoxaline	TCQ	1 min	100
Halogenated Triazines			
atrazine	Atraz	4.3 days	100
fluoroatrazine	Fatrz	6.1 days	100
cyanazine	Cyaz	3.1 days	88
anilazine	Anlz	<1 min	99

^a These values represent the maximum concentrations of these reduced sulfur species reported for Great Marsh, DE sediment porewaters (9). ^b $[\text{HS}^-]$ calculated from 5.06 mM $[\text{H}_2\text{S}]_{\text{T}}$ at pH 7.2. ^c $t_{1/2} = 0.693/(k_{\text{S}_n^{2-}}\Sigma[\text{S}_n^{2-}] + k_{\text{HS}^-}[\text{HS}^-])$. ^d Computed as $100 \times k_{\text{S}_n^{2-}}\Sigma[\text{S}_n^{2-}]/(k_{\text{S}_n^{2-}}\Sigma[\text{S}_n^{2-}] + k_{\text{HS}^-}[\text{HS}^-])$.

of HS^- and polysulfides reported (9) for salt marsh porewaters. The results (Table 2) range from less than 1 min for the highly reactive anilazine and TCPm to greater than 1.5 years for DCP. Note that even though the concentration of polysulfides is an order of magnitude less than the bisulfide concentration (0.33 versus 3.4 mM, respectively), polysulfides were still predicted to account for more than 97% of the overall rate of reaction (with the exception of cyanazine, for which the contribution of polysulfides was predicted to be 88%). This reflects the very high nucleophilicity of polysulfides in S_nAr reactions with chloroazines.

The chloroazine agrochemicals react readily with polysulfide species to form sulfur-substituted triazine products, as identified by GC/MS analysis of methylated and pentafluorobenzylation derivatives. The polymercaptoazine products believed to result initially from nucleophilic displacement of chloride could not be identified directly by the analytical techniques employed in this study. Nor were we able to determine whether the polysulfide chains were cleaved immediately following reaction with S_n^{2-} or during derivatization. Direct observation of polysulfide-substituted products, which would help to resolve this issue, may require alternative analytical methods, such as liquid chromatography/mass spectrometry (LC/MS) employing a relatively soft ionization technique.

Whether these products are charged or neutral under environmentally relevant conditions will influence their interactions with biota and hence their (eco)toxicity. Our inability to extract (into *n*-hexane) underivatized products of polysulfide reaction with azines might suggest them to be charged, although we note that the neutral species hydroxyatrazine (which occurs principally as the keto tautomer at neutral pH; see ref 56) extracts poorly into *n*-hexane. The relatively high dissociation constants reported for mercapto-substituted aminopyrimidines (e.g., pK_a of 10.45 for 4,6-diamino-2-mercaptopyrimidine; see ref 57) suggest that the mercapto-substituted products of chloro-*s*-triazine reaction could be protonated (and hence neutral) at environmental pH values.

The extent to which the sulfur-substituted reaction products undergo tautomerization may influence their reactivity with naturally occurring alkylating agents (e.g., $\text{CH}_3\text{-Br}$ or CH_3I ; see ref 58). Mercaptopyrimidines (59) have been

demonstrated to undergo tautomerization to the thione form in aqueous solution. The length of the polysulfide chain within the azine substitution products would dictate whether such tautomerization reactions would occur; aryl disulfide ions (ArS_2^-) have been reported to be 10 times more reactive toward alkyl halides in dimethylacetamide than the corresponding arylmonosulfide ions (ArS^-) (60).

If alkylthiotriazines were to form through reaction of mercaptotriazines with methyl halides, they may prove less persistent than the parent halotriazines (61). Triazine herbicides containing methylthio groups (e.g., ametryn, prometryn, simetryn) in place of the chloro substituents are, however, known to be toxic to aquatic organisms. Indeed, ametryn is more toxic to fish than is its chlorinated analogue, atrazine (39). That chlorotriazine herbicides react readily with reduced sulfur nucleophiles may indicate a need for future (eco)toxicological assessments.

Acknowledgments

Urs Jans performed preliminary investigations into reactions of 2,3-dichloroquinoxaline with reduced sulfur species. Michelle Hladik conducted S_8 analyses on pentane extracts of Na_2S_4 solutions and assisted in analyses of methylated polysulfide solutions. We are also grateful for the comments of two anonymous reviewers. Although the research described herein has been funded in part by the United States Environmental Protection Agency through Grant R826269-01-0, it has not been subjected to the Agency's required peer and policy review and therefore does not necessarily reflect the views of the Agency, and no official endorsement should be inferred. Additional funding was provided by an NSF Young Investigator Award (Grant BES-9457260) to A.L.R. in addition to a dissertation fellowship (1999–2000) to K.A.L. granted by the American Association of University Women.

Supporting Information Available

Tables showing compositions of polysulfide solutions used to determine second-order rate constants for reaction of atrazine, a list of products tentatively identified by GC/MS for reactions of haloazines with HS^- and S_n^{2-} , figures showing the predicted speciation of polysulfides, and mass spectra of methylated products obtained for reaction of cyanazine with S_n^{2-} and for reaction of anilazine with HS^- and S_n^{2-} are provided. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Received for review August 28, 2001. Revised manuscript received February 1, 2002. Accepted February 13, 2002.

ES011255V